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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/525,259	02/22/2005	Margaret Sin Ka Wan	13404US	5000
7590 Battelle Memorial Institute 505 King Avenue Columbus, OH 43201-2693			EXAMINER FERNANDEZ, SUSAN EMILY	
			ART UNIT 1651	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/525,259

Applicant(s)

WAN, MARGARET SIN KA

Examiner

SUSAN E. FERNANDEZ

Art Unit

1651

Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 April 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-30, 35, 36 and 49-53 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-30, 35, 36 and 49-53 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB-08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on April 14, 2008, has been entered.

Claims 31-34 and 37-48 are cancelled. Claims 1-30, 35, 36, and 49-53 are pending and examined on the merits to the extent they read on the elected invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-30, 35, 36, and 49-53 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 14, 16, 18, 20, 21, and 24 are indefinite since it is unclear that the liquid comprising biologically compatible polymer supplied to a liquid outlet is the same liquid issuing from the outlet. Thus, claims 1-30, 35, 36, and 49-53 are rejected under 35 U.S.C. 112, second paragraph.

Claim 1 is rendered indefinite by the recitation "...selecting a size of the gaps...and a size of the fibre diameter..." since it is unclear that the size of the gaps and the size of the fibre diameter of the fibre scaffold is limited only to these selected gap and fibre diameter sizes. The

use of the term "a size" seems to signify that there are other sizes present. Thus, claims 1-13, 22, 23, 27-30, 35, 36, and 49 are rejected under 35 U.S.C. 112, second paragraph.

Additionally, claim 14 is rendered indefinite by the recitation "...selecting a size of the gaps between the fibre portions" since it is unclear that the gap sizes are limited to the selected size. The use of the term "a size" seems to signify that there are other sizes present.

Claim 16 is rendered indefinite by the recitation "...selecting a fibre diameter and a gap between fibre portions..." since it is unclear that the fibre diameter and gap sizes are limited solely to these selected sizes. The use of the terms "a fibre diameter" and "a gap" seems to signify that other diameters and gaps are present. Thus, claims 16, 17, 19, 50, and 51 are rejected under 35 U.S.C. 112, second paragraph.

Claim 18 is rendered indefinite by the recitation "...selecting a fibre diameter" since it is unclear that the fibre diameter is limited solely to the selected size given the use of the term "a fibre diameter." Furthermore, claim 18 is rendered indefinite by the recitation "...the selecting of the fibre diameter and gaps resulting, after a period of time, in the cells having a morphology resembling nerve cells." It is unclear how the selection step itself can affect the cell morphology.

Claims 20 and 21 are rendered indefinite by the recitation "...selecting a fibre diameter...and a gap size..." since it is unclear that the fibre diameter and gap size are limited solely to those sizes given the use of the terms "a fibre diameter" and "a gap size." Furthermore, it is unclear how the selection step itself facilitates at least once cell process. Thus, claims 15, 20, and 21 are rejected under 35 U.S.C. 112, second paragraph.

Claim 24 is rendered indefinite by the recitation "selecting...a fibre diameter...and a gap size" since it is unclear that the fibre diameter and gap size are limited solely to those sizes

given the use of the terms “a fibre diameter” and “a gap size.” Thus, claims 24-26 are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-18, 20-28, 35, 36, and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shastri et al. (WO 97/16545) in view of Coffee et al. (WO 98/03267), Sussman et al. (US 5,266,476), and Leong et al. (US 5,686,091).

Shastri et al. discloses a method for altering the regeneration, differentiation, or function of cells (claim 1), wherein cells are attached to a surface comprising an electrically conducting polymer (such as a biocompatible polymer, see claim 10). See also the abstract which indicates that conductive polymers are seeded with nerve cells. As indicated at page 15, lines 13-19, the electrically conducting polymer should be porous, where the pores should allow for vascular ingrowth and the seeding of cells without damage to the cells or patient, said pores generally in the range of between approximately 100 and 300 microns. Further still, the Shastri invention can be used to alter the regeneration, differentiation, or function of cells including various “organ cells”, muscles cells, and “cells forming bone and cartilage” (page 18, lines 24-27).

Shastri et al. differs from the claimed reference in that it does not expressly disclose that the polymer on which the cells are attached is a fibre scaffold created by supplying a liquid

comprising the biologically compatible polymer to a liquid outlet in the vicinity of a surface and subjecting the liquid issuing from the outlet to an electric field to cause the liquid to form polymer fibre which is attracted to and deposits onto the surface.

Coffee et al. discloses a method of depositing fibres on a surface wherein a liquid comprising a biocompatible polymer is subjected to an electrohydrodynamic process in the vicinity of said surface (page 4, third paragraph). See Figure 1. Thus, Coffee et al. discloses supplying liquid comprising compatible polymer to a liquid outlet in the vicinity of a surface and subjecting liquid issuing from the outlet to an electric field to cause the liquid to form polymer fibres which are attracted to and deposit onto the surface to form a polymer fibre scaffold, as required by certain limitations in parent claims 1, 14, 16, 18, 20, 21, and 24. Given that the Coffee method can be used to form a mat or web of fibres (page 21, last paragraph, and Figure 9), Coffee et al. teaches the creation of a three-dimensional continuous network of intercommunicating fibre portions.

Additionally, Coffee et al. teaches that the fibres can have a diameter in the range of 10 nm to above 100 microns (page 17, first paragraph, second to last sentence), which meets the diameter limitation of instant claim 7. Further still, the reference teaches that the liquid comprising a biocompatible polymer can be a solution or a melt (page 22, last paragraph) and the polymer can be polylactic acid (polylactide) (page 4, second paragraph) or “New Skin” wherein the fibres formed are approximately 0.5 to 5 microns in diameter (page 19, last paragraph). Thus, limitations in instant claims 10, 22, and 23 are disclosed in the reference. Also, the limitations of instant claims 25, 26, 49, 52, and 53 are taught by Coffee et al. (page 4, second paragraph and third paragraph).

At the time the invention was made, it would have been obvious to have used the polymer fibre scaffold disclosed in Coffee et al. as the polymer serving for cell attachment of the Shastri invention. One of ordinary skill in the art would have been motivated to do this since the Coffee polymer fibre scaffold provides biocompatible polymer as required by the Shastri invention. Furthermore, the methods of Coffee et al. provides for formation of fibres, thus allowing for formation of pores. As pointed out in Shastri et al, a matrix for implantation to form new tissue should be pliable, non-toxic, porous template for vascular ingrowth, wherein the pores should allow vascular ingrowth and the seeding of cells (page 15, lines 13-18). Furthermore, it would have been obvious that the regeneration, differentiation, or function would have been altered of any type of cells, including human adherent cells, human fibroblast cells, and stem cells. Thus, the cell types recited in claims 11-14 and 16-18 (and the preamble of parent claims 1, 14, 16, 18, 20, 21, and 24) are rendered obvious.

The references differ from the claimed invention in that they do not expressly disclose selecting a fibre diameter and a size of the gaps between the fibre portions that facilitate a cell process.

Sussman et al. discloses a fibrous matrix for attachment of cells (abstract). For adequate porosity for cell entrance, entrance of nutrients, and for removal of waste products from the fibrous matrix, the pores have a particular diameter and are prepared by using fibers having diameters ranging from about 0.5 to 20 microns (column 4, lines 55-66).

Leong et al. discloses a biodegradable foam scaffold for cell transplantation featuring a continuous network of pores (abstract). Leong et al. points out that "...the vascularization and nature of tissue ingrowth depend on the pore diameter and interconnecting structure" (column 3,

lines 43-45). Cells seeded onto the biodegradable foam scaffold generally range from about 7-15 microns in diameter, and include a variety of cells types, including fibroblasts (column 5, lines 24-29).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have varied the gap distance between the fibres in the Coffee scaffold to other gap distances, including those recited in the instant claims, through routine experimentation. Furthermore, one of ordinary skill in the art would have been motivated to do this since Sussman et al. and Leong et al. demonstrate that the gap size affects cell entrance, entrance of nutrients, removal of waste products, vascularization, and nature of tissue ingrowth. Also, it would have been obvious to have used fibre diameters included in the range recited in Sussman et al., which meet the fibre diameter limitation in instant claim 6, since it would have resulted in fibrous matrix pore sizes suitable for cell entrance, entrance of nutrients, and removal of waste products. Given that vascularization and the nature of tissue ingrowth is affected by the pore and fibre diameter sizes, the cell processes recited in the instant claims are facilitated. Furthermore, it would have been obvious to have used cells of the sizes recited in Leong et al. since such cells are suitable for seeding in scaffolds, resulting in vascularization and tissue ingrowth. Thus, claims 2-6, 8, and 9 are also rendered obvious.

A holding of obviousness is clearly required.

Claims 1-30, 35, 36, and 49-53 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shastri et al., Coffee et al., Sussman et al., and Leong et al. as applied to claims 1-18, 20-28,

35, 36, and 49-53 above, and further in view of Smith et al. (WO 01/27365) and Simpson et al. (WO 02/40242).

As discussed above, Shastri et al., Coffee et al., Sussman et al., and Leong et al. render claims 1-18, 20-28, 35, 36, and 49-53 obvious. However, these references do not expressly disclose that the polymer used is polycaprolactone.

Smith et al. discloses that polycaprolactone is a polymer suitable for making fiber wherein a polymer solution in a liquid jet is introduced into an electric field and formed and elongated on a surface, such as a wound (page 11, lines 4-6, page 14, lines 17-20, and page 17, lines 14-20).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have created the fibre scaffold rendered obvious by the references with a solution comprising polycaprolactone. One of ordinary skill in the art would have been motivated to do this since polycaprolactone is a polymer which can form fibres on a surface when exposed to an electric field. Thus, further limitations of claims 10 and 14, and claim 19 are rendered obvious by the references.

Additionally, the references differ from the claimed invention in that they do not teach preparing a liquid formulation comprising cell culture medium with a water soluble polymer, or that this liquid formulation is exposed to an electric field to cause the liquid to break into droplets or to form at least one fibre.

Simpson et al. discloses using mixed solutions (nonbiological but biologically compatible material along with substances such as cells) in electroprocessing, wherein fibres or droplets are formed composed of electroprocessed materials as well as one or more substances (page 33, lines

25-28). Electroprocessing is streaming, spraying, sputtering or dripping material across an electric field and toward a target (page 6, lines 37-40).

At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to have introduced mammalian cells by combining a cell culture with a polymer for the formation of fibres by electroprocessing when conducting the invention rendered obvious by the references. One of ordinary skill in the art would have been motivated to do this since this technique is appropriate for delivering cells to an electroprocessed polymer and further would allow formation of fibres as required by Coffee et al. Thus, claims 29 and 30 are rendered obvious.

Note further that Simpson et al. provides further motivation for applying mammalian cells to the fibre scaffold rendered obvious by the references as Simpson et al. teaches combining cells with an electroprocessed collagen matrix in order to provide scaffolding or seeding for the formation of engineered tissue, where the cells include stems cells and fibroblasts (page 17, lines 19-32 and abstract).

A holding of obviousness is clearly required.

Response to Arguments

Applicant's arguments filed April 14, 2008, have been fully considered but they are not persuasive. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Coffee et al. is provided to demonstrate the process by which a fibre scaffold is produced using a liquid outlet, biologically compatible polymer, and an electric field. However, Shastri et al., Sussman et al., and Leong et al. show that a porous scaffold is used for the seeding of cells. It is noted that Shastri is provided to show that a biologically compatible polymer with pores is used for cell seeding. Though the selection of gap size and fibre diameter is a matter of routine optimization, Sussman et al. and Leong et al. are new references cited to provide evidence that gap size, which is linked to fiber diameter, facilitates cellular processes and therefore gap size and fibre diameter are selected for that purpose. Even Shastri et al. points out that the pores allow for vascular ingrowth, and thus facilitate cell processes, including differentiation, as required by the claims.

With respect to Shastri et al., the applicant asserts that it teaches that the substrate does not even have to be porous, let alone fibrous. However, page 15 of Shastri et al. states that "a matrix for implantation to form new tissue should be a pliable, non-toxic, porous template for vascular ingrowth." Clearly the Shastri invention is not limited solely to non-porous substrates. Moreover, Sussman et al. and Leong et al. provide further support for using a porous (fibrous) scaffold.

The applicant also argues that neither Coffee et al. nor Shastri et al. teaches anything about the relationship between fibre diameter and fibre gap. However, it is noted that the features upon which applicant relies (i.e., relationship between fibre diameter and fibre gap) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Smith et al. is only provided to show that polycaprolactone is suitable for use in creation of a fibre scaffold as taught by the methods of Coffee et al, and Simpson et al. is provided to demonstrate that biologically compatible material along with cells can be electroprocessed.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SUSAN E. FERNANDEZ whose telephone number is (571)272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leon B Lankford/
Primary Examiner, Art Unit 1651

Susan E. Fernandez
Examiner
Art Unit 1651

sef